POTASSIUM CHLORIDE - potassium chloride tablet, film coated, extended release
Physicians Total Care, Inc.

Potassium
Chloride
Extended-release Tablets, USP
8 mEq and 10 mEq

DESCRIPTION

Potassium Chloride Extended-release Tablets, USP are a solid oral dosage form of potassium chloride. Each contains 600 mg or 750 mg of potassium chloride equivalent to 8 mEq or 10 mEq of potassium in a wax matrix tablet. This formulation is intended to provide an extended-release of potassium from the matrix to minimize the likelihood of producing high, localized concentrations of potassium within the gastrointestinal tract.

Potassium Chloride Extended-release Tablets are an electrolyte replenisher. The chemical name is potassium chloride, and the structural formula is KCl. Potassium chloride, USP is a white, granular powder or colorless crystals. It is odorless and has a saline taste. Its solutions are neutral to litmus. It is freely soluble in water and insoluble in alcohol.

Inactive Ingredients

Hydrogenated vegetable oil, magnesium stearate, polyethylene glycol, polyvinyl alcohol, silicon dioxide, talc and titanium dioxide. Dark blue tablets also contain FD&C Blue No. 1 aluminum lake.

CLINICAL PHARMACOLOGY

The potassium ion is the principal intracellular cation of most body tissues. Potassium ions participate in a number of essential physiological processes including the maintenance of intracellular tonicity, the transmission of nerve impulses, the contraction of cardiac, skeletal and smooth muscle and the maintenance of normal renal function.

The intracellular concentration of potassium is approximately 150 to 160 mEq per liter. The normal adult plasma concentration is 3.5 to 5 mEq per liter. An active ion transport system maintains this gradient across the plasma membrane.

Potassium is a normal dietary constituent and under steady state conditions the amount of potassium absorbed from the gastrointestinal tract is equal to the amount excreted in the urine. The usual dietary intake of potassium is 50 to 100 mEq per day.

Potassium depletion will occur whenever the rate of potassium loss through renal excretion and/or loss from the gastrointestinal tract exceeds the rate of potassium intake. Such depletion usually develops slowly as a consequence of prolonged therapy with oral diuretics, primary or secondary hyperaldosteronism, diabetic ketoacidosis, severe diarrhea, or inadequate replacement of potassium in patients on prolonged parenteral nutrition. Depletion can develop rapidly with severe diarrhea, especially if associated with vomiting. Potassium depletion due to these causes is usually accompanied by a concomitant loss of chloride and is manifested by hypokalemia and metabolic alkalosis. Potassium depletion may produce weakness, fatigue, disturbances of cardiac rhythm (primarily ectopic beats), prominent U-waves in the electrocardiogram and, in advanced cases, flaccid paralysis and/or impaired ability to concentrate urine.

If potassium depletion associated with metabolic alkalosis cannot be managed by correcting the fundamental cause of the deficiency, e.g., where the patient requires long term diuretic therapy, supplemental potassium in the form of high potassium food or potassium chloride may be able to

restore normal potassium levels.

In rare circumstances (e.g., patients with renal tubular acidosis) potassium depletion may be associated with metabolic acidosis and hyperchloremia. In such patients potassium replacement should be accomplished with potassium salts other than the chloride, such as potassium bicarbonate, potassium citrate, potassium acetate or potassium gluconate.

The potassium chloride in Potassium Chloride Extended-release Tablets is completely absorbed before it leaves the small intestine. The wax matrix is not absorbed and is excreted in the feces; in some instances the empty matrices may be noticeable in the stool. When the bioavailability of the potassium ion from the Potassium Chloride Extended-release Tablets is compared to that of a true solution the extent of absorption is similar.

The extended-release properties of Potassium Chloride Extended-release Tablets are demonstrated by the finding that a significant increase in time is required for renal excretion of the first 50% of the Potassium Chloride Extended-release Tablets dose as compared to the solution.

Increased urinary potassium excretion is first observed 1 hour after administration of Potassium Chloride Extended-release Tablets, reaches a peak at approximately 4 hours, and extends up to 8 hours. Mean daily steady-state plasma levels of potassium following daily administration of Potassium Chloride Extendedrelease Tablets cannot be distinguished from those following administration of potassium chloride solution or from control plasma levels of potassium ion.

INDICATIONS AND USAGE

BECAUSE OF REPORTS OF INTESTINAL AND GASTRIC ULCERATION AND BLEEDING WITH EXTENDED-RELEASE POTASSIUM CHLORIDE PREPARATIONS, THESE DRUGS SHOULD BE RESERVED FOR THOSE PATIENTS WHO CANNOT TOLERATE OR REFUSE TO TAKE LIQUID OR EFFERVESCENT POTASSIUM PREPARATIONS OR FOR PATIENTS IN WHOM THERE IS A PROBLEM OF COMPLIANCE WITH THESE PREPARATIONS.

1. For the therapeutic use of patients with hypokalemia, with or without metabolic alkalosis; in digitalis intoxication; and in patients with hypokalemic familial periodic paralysis. If hypokalemia is the result of diuretic therapy, consideration should be given to the use of a lower dose of diuretic, which may be sufficient without leading to hypokalemia.
2. For the prevention of hypokalemia in patients who would be at particular risk if hypokalemia were to develop, e.g., digitalized patients or patients with significant cardiac arrhythmias.

The use of potassium salts in patients receiving diuretics for uncomplicated essential hypertension is often unnecessary when such patients have a normal dietary pattern and when low doses of the diuretic are used. Serum potassium should be checked periodically, however, and if hypokalemia occurs, dietary supplementation with potassium-containing foods may be adequate to control milder cases. In more severe cases, and if dose adjustment of the diuretic is ineffective or unwarranted, supplementation with potassium salts may be indicated.

CONTRAINDICATIONS

Potassium supplements are contraindicated in patients with hyperkalemia since a further increase in serum potassium concentration in such patients can produce cardiac arrest. Hyperkalemia may complicate any of the following conditions: chronic renal failure, systemic acidosis such as diabetic acidosis, acute dehydration, extensive tissue breakdown as in severe burns, adrenal insufficiency or the administration of a potassiumsparing diuretic (e.g., spironolactone, triamterene or amiloride) (see **OVERDOSAGE**).

Extended-release formulations of potassium chloride have produced esophageal ulceration in certain cardiac patients with esophageal compression due to an enlarged left atrium. Potassium supplementation,

when indicated in such patients, should be given as a liquid preparation.

All solid oral dosage forms of potassium chloride are contraindicated in any patient in whom there is structural, pathological (e.g., diabetic gastroparesis) or pharmacologic (use of anticholinergic agents or other agents with anticholinergic properties at sufficient doses to exert anticholinergic effects) cause for arrest or delay in tablet passage through the gastrointestinal tract.

WARNINGS

Hyperkalemia

(see **OVERDOSAGE**)

In patients with impaired mechanisms for excreting potassium, the administration of potassium salts can produce hyperkalemia and cardiac arrest. This occurs most commonly in patients given potassium by the intravenous route but may also occur in patients given potassium orally. Potentially fatal hyperkalemia can develop rapidly and be asymptomatic.

The use of potassium salts in patients with chronic renal disease, or any other condition which impairs potassium excretion, requires particularly careful monitoring of the serum potassium concentration and appropriate dosage adjustment.

Interaction with Potassium-sparing Diuretics

Hypokalemia should not be treated by the concomitant administration of potassium salts and a potassium-sparing diuretic (e.g., spironolactone, triamterene or amiloride), since the simultaneous administration of these agents can produce severe hyperkalemia.

Interaction with Angiotensin Converting Enzyme Inhibitors

Angiotensin converting enzyme (ACE) inhibitors (e.g., captopril, enalapril) will produce some potassium retention by inhibiting aldosterone production. Potassium supplements should be given to patients receiving ACE inhibitors only with close monitoring.

Gastrointestinal Lesions

Solid oral dosage forms of potassium chloride can produce ulcerative and/or stenotic lesions of the gastrointestinal tract. Based on spontaneous adverse reaction reports, enteric-coated preparations of potassium chloride are associated with an increased frequency of small bowel lesions (40-50 per 100,000 patient years) compared to extended-release wax matrix formulations (less than one per 100,000 patient years). Because of the lack of extensive marketing experience with microencapsulated products, a comparison between such products and wax matrix or enteric-coated products is not available. Potassium Chloride Extended-release Tablets are wax matrix tablets formulated to provide an extended rate of release of potassium chloride and thus to minimize the possibility of high local concentration of potassium near the gastrointestinal wall.

Prospective trials have been conducted in normal human volunteers in which the upper gastrointestinal tract was evaluated by endoscopic inspection before and after one week of solid oral potassium chloride therapy. The ability of this model to predict events occurring in usual clinical practice is unknown. Trials which approximated usual clinical practice did not reveal any clear differences between the wax matrix and microencapsulated dosage forms. In contrast, there was a higher incidence of gastric and duodenal lesions in subjects receiving a high dose of a wax matrix extended-release formulation under conditions which did not resemble usual or recommended clinical practice (i.e., 96 mEq per day in divided doses of potassium chloride administered to fasted patients, in the presence of an anticholinergic drug to delay gastric emptying). The upper gastrointestinal lesions observed by endoscopy were asymptomatic and were not accompanied by evidence of bleeding (hemoccult testing). The relevance of these findings to the usual conditions (i.e., non-fasting, no anticholinergic agent,

smaller doses) under which extended-release potassium chloride products are used is uncertain; epidemiologic studies have not identified an elevated risk, compared to microencapsulated products, for upper gastrointestinal lesions in patients receiving wax matrix formulations. Potassium Chloride Extendedrelease Tablets should be discontinued immediately and the possibility of ulceration, obstruction or perforation considered if severe vomiting, abdominal pain, distention or gastrointestinal bleeding occurs.

Metabolic Acidosis

Hypokalemia in patients with metabolic acidosis should be treated with an alkalinizing potassium salt such as potassium bicarbonate, potassium citrate, potassium acetate or potassium gluconate.

PRECAUTIONS

General

The diagnosis of potassium depletion is ordinarily made by demonstrating hypokalemia in a patient with a clinical history suggesting some cause for potassium depletion. In interpreting the serum potassium level, the physician should be aware that acute alkalosis *per se* can produce hypokalemia in the absence of a deficit in total body potassium while acute acidosis *per se* can increase the serum potassium concentration into the normal range even in the presence of a reduced total body potassium. The treatment of potassium depletion, particularly in the presence of cardiac disease, renal disease or acidosis requires careful attention to acid-base balance and appropriate monitoring of serum electrolytes, the electrocardiogram and the clinical status of the patient.

Information for Patients

Physicians should consider reminding the patient of the following:

- To take each dose with meals and with a full glass of water or other liquid.
- To take this medicine following the frequency and amount prescribed by the physician. This is especially important if the patient is also taking diuretics and/or digitalis preparations.
- To check with the physician if there is trouble swallowing the tablets or if the tablets seem to stick in the throat.
- To check with the physician at once if tarry stools or other evidence of gastrointestinal bleeding is noticed.
- To take each dose without crushing, chewing or sucking the tablets.

Laboratory Tests

When blood is drawn for analysis of plasma potassium it is important to recognize that artifactual elevations can occur after improper venipuncture technique or as a result of *in vitro* hemolysis of the sample.

Drug Interactions

Potassium-sparing diuretic, angiotensin converting enzyme inhibitors (see **WARNINGS**).

Carcinogenesis, Mutagenesis, Impairment of Fertility

Carcinogenicity, mutagenicity and fertility studies in animals have not been performed. Potassium is a normal dietary constituent.

Pregnancy

Pregnancy Category C

Animal reproduction studies have not been conducted with Potassium Chloride Extended-release Tablets. It is unlikely that potassium supplementation that does not lead to hyperkalemia would have an adverse effect on the fetus or would affect reproductive capacity.

Nursing Mothers

The normal potassium ion content of human milk is about 13 mEq per liter. It is not known if Potassium Chloride Extended-release Tablets have an effect on this content. Since oral potassium becomes part of the body potassium pool, so long as body potassium is not excessive, the contribution of potassium chloride supplementation should have little or no effect on the level in human milk.

Pediatric Use

Safety and effectiveness in the pediatric population have not been established.

Geriatric Use

Clinical studies of Potassium Chloride Extended-release Tablets did not include sufficient numbers of subjects aged 65 and over to determine whether they respond differently from younger subjects. Other reported clinical experience has not identified differences in responses between the elderly and younger patients. In general, dose selection for an elderly patient should be cautious, usually starting at the low end of the dosing range, reflecting the greater frequency of decreased hepatic, renal or cardiac function, and of concomitant disease or other drug therapy.

This drug is known to be substantially excreted by the kidney, and the risk of toxic reactions to this drug may be greater in patients with impaired renal function. Because elderly patients are more likely to have decreased renal function, care should be taken in dose selection, and it may be useful to monitor renal function.

ADVERSE REACTIONS

One of the most severe adverse effects is hyperkalemia (see **CONTRAINDICATIONS, WARNINGS** and **OVERDOSAGE**). There also have been reports of upper and lower gastrointestinal conditions including obstruction, bleeding, ulceration and perforation (see **CONTRAINDICATIONS** and **WARNINGS**).

The most common adverse reactions to oral potassium salts are nausea, vomiting, flatulence, abdominal pain/discomfort and diarrhea. These symptoms are due to irritation of the gastrointestinal tract and are best managed by taking the dose with meals or reducing the amount taken at one time.

Skin rash has been reported rarely.

OVERDOSAGE

The administration of oral potassium salts to persons with normal excretory mechanisms for potassium rarely causes serious hyperkalemia. However, if excretory mechanisms are impaired, or if potassium is administered too rapidly intravenously, potentially fatal hyperkalemia can result (see **CONTRAINDICATIONS** and **WARNINGS**). It is important to recognize that hyperkalemia is usually asymptomatic and may be manifested only by an increased serum potassium concentration (6.5-8.0 mEq/L) and characteristic electrocardiographic changes (peaking of T-waves, loss of P-wave, depression of S-T segment and prolongation of the QT interval). Late manifestations include muscle paralysis and cardiovascular collapse from cardiac arrest (9-12 mEq/L).

Treatment measures for hyperkalemia include the following:

1. Elimination of foods and medications containing potassium and of any agents with potassium-sparing properties.
2. Intravenous administration of 300 to 500 mL/hr of 10% dextrose solution containing 10-20 units of

crystalline insulin per 1,000 mL.
3. Correction of acidosis, if present, with intravenous sodium bicarbonate.
4. Use of exchange resins, hemodialysis or peritoneal dialysis.

In treating hyperkalemia, it should be recalled that in patients who have been stabilized on digitalis, too rapid a lowering of the serum potassium concentration can produce digitalis toxicity.

The extended release feature means that absorption and toxic effects may be delayed for hours. Consider standard measures to remove any unabsorbed drug.

DOSAGE AND ADMINISTRATION

The usual dietary potassium intake by the average adult is 50 to 100 mEq per day. Potassium depletion sufficient to cause hypokalemia usually requires the loss of 200 mEq or more of potassium from the total body store.

Dosage must be adjusted to the individual needs of each patient. The dose for the prevention of hypokalemia is typically in the range of 20 mEq per day. Doses of 40-100 mEq per day or more are used for the treatment of potassium depletion. Dosage should be divided if more than 20 mEq per day is given such that no more than 20 mEq is given in a single dose.

Each Potassium Chloride Extended-release Tablet provides 8 mEq or 10 mEq of potassium chloride.

Potassium Chloride Extended-release Tablets should be taken with meals and with a glass of water or other liquid. This product should not be taken on an empty stomach because of its potential for gastric irritation (see **WARNINGS**).

NOTE: Potassium Chloride Extended-release Tablets must be swallowed whole and never crushed, chewed or sucked.

HOW SUPPLIED

Film-coated Potassium Chloride 8 mEq (dark-blue, debossed with "USL 8"), Potassium Chloride 10 mEq (white, debossed with "USL 10"), round tablets containing:

600 mg potassium chloride (equivalent to 8 mEq) in

Bottles of 30	NDC 54868-0097-2
Bottles of 100	NDC 54868-0097-4

Store at controlled room temperature, 15-30°C (59-86°F). Protect from light and moisture. Dispense in a tight container with child-resistant closure.

Manufactured by
UPSHER-SMITH LABORATORIES, INC.
Minneapolis, MN 55447
for
Sandoz Inc.
Princeton, NJ 08540

Revised 0809

Relabeling and Repackaging by:
Physicians Total Care, Inc.
Tulsa, Oklahoma 74146

PRINCIPAL DISPLAY PANEL - 600 mg Tablet Bottle Label

Potassium Chloride
Extended-Release
Tablets, USP

8 mEq (600 mg)

R_x only

POTASSIUM CHLORIDE

potassium chloride tablet, film coated, extended release

Product Information			
Product Type	HUMAN PRESCRIPTION DRUG	**Item Code (Source)**	NDC:54868-0097(NDC:0781-1516)
Route of Administration	ORAL		

Active Ingredient/Active Moiety		
Ingredient Name	**Basis of Strength**	**Strength**
Potassium Chloride (UNII: 660YQ98I10) (Potassium Cation - UNII:295O53K152)	Potassium Chloride	600 mg

Inactive Ingredients	
Ingredient Name	**Strength**
hydrogenated cottonseed oil (UNII: Z82Y2C65EA)	
magnesium stearate (UNII: 70097M6I30)	
polyethylene glycols (UNII: 3WJQ0SDW1A)	
polyvinyl alcohol (UNII: 532B59J990)	
silicon dioxide (UNII: ETJ7Z6XBU4)	
talc (UNII: 7SEV7J4R1U)	
titanium dioxide (UNII: 15FIX9V2JP)	
FD&C BLUE NO. 1 (UNII: H3R47K3TBD)	

Product Characteristics			
Color	BLUE (dark blue)	**Score**	no score
Shape	ROUND	**Size**	11mm
Flavor		**Imprint Code**	USL;8
Contains			

Packaging

#	Item Code	Package Description	Marketing Start Date	Marketing End Date
1	NDC:54868-0097-2	30 in 1 BOTTLE		
2	NDC:54868-0097-4	100 in 1 BOTTLE		

Marketing Information

Marketing Category	Application Number or Monograph Citation	Marketing Start Date	Marketing End Date
NDA	NDA019123	10/01/1996	

Labeler - Physicians Total Care, Inc. (194123980)

Establishment

Name	Address	ID/FEI	Business Operations
Physicians Total Care, Inc.		194123980	relabel, repack

Revised: 4/2012 Physicians Total Care, Inc.